



UNITED STATES PATENT AND TRADEMARK OFFICE

WJD
UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/870,375 | 05/30/2001 | Veronique Gruber | 18433/2022 | 7238 |
| 29933 | 7590 | 04/09/2004 | EXAMINER | |
| PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199 | | | LAMBERTSON, DAVID A | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1636 | |

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/870,375 | GRUBER ET AL. |
| | Examiner | Art Unit |
| | David A. Lambertson | 1636 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 02 January 2004.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-61 is/are pending in the application.
 4a) Of the above claim(s) 4,31,33 and 37-45 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-3,5-30,32,34-36 and 46-61 is/are rejected.
 7) Claim(s) 57,59 and 61 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 22 in the response filed January 2, 2004 is acknowledged. The traversal is on the ground(s) that SEQ ID NO: 4, 21 and 22 are indeed related and would not present an undue search burden because: (a) each group has at least one copy of a G-box and an enhancer; and (b) due to the similarity between the functional elements of these sequences, a search of one sequence would necessarily uncover all three promoters.

This is not found persuasive because of the following reasons:

1. As established in the previous Election/Restriction Action, the Commissioner has acknowledged that a single nucleotide sequence represents a single invention. Since SEQ ID NO: 4, 21 and 22 are not identical, they represent different inventions, and therefore are properly restricted.
2. Applicant's assertion that a search of the functional elements would necessarily result in the identification of each of the sequences does not appear to be substantiated. For example, consider the comparison of SEQ ID NO: 4 and the elected sequence SEQ ID NO: 22- the full 35 nucleotides of SEQ ID NO: 22 appears nowhere in SEQ ID NO: 4; indeed, among the first 8 nucleotides of SEQ ID NO: 22, there is not even a stretch of 4 nucleotides that has 100% identity to SEQ ID NO: 4 (i.e., the sequences atcg, tcgg, cgga, ggaa, gaat do not appear anywhere in SEQ ID NO: 4). Based on this brief analysis of SEQ ID NO: 22 relative to SEQ ID NO: 4, one would realize that there are substantial differences between the two sequences that require each of the sequences to be separately searched. Thus, two distinct and independent searches are required to

accurately search the inventions, and said searches would be burdensome to the Office because a single invention should only require a single search.

In conclusion, there is no way to perform a single search of either SEQ ID NO: 4, 21 or 22 and necessarily obtain art that reads on all three of the sequences because the sequences are not identical. As a result, multiple searches would be required to search Applicant's version of a single invention, and these multiple searches would be unduly burdensome. As a result, the requirement is still deemed proper and is therefore made FINAL.

It is noted that the claims set forth as linking claims in the Election/Restriction Requirement have been rejected, and, as a consequence of their non-allowability, the inventions will not be rejoined through the linking claims.

Claims 1-61 are pending in the instant Application. Claims 4, 31, 33 and 37-45 are withdrawn as being drawn to a non-elected invention. Claims 1-3, 5-30, 32, 34-36 and 46-61 are under examination in the instant application.

Priority

Applicant's claim for priority to PCT/IB00/01383 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed March 10, 2003 has been considered, and a signed and initialed copy of the form PTO-1449 has been attached to this Office Action.

Specification

The specification is not in sequence compliance because the specification contains sequences that require identification by SEQ ID NOS. Specifically, these sequences appear on pages 22-25 and 27-43. It appears that each of these sequences is properly set forth in the Sequence Listing, therefore the lack of compliance does not preclude the examination of the application. However, a complete response to this Office Action requires that the specification be properly amended to refer to the SEQ ID NOS for each of these sequences.

Additionally, page 71 (the claims) should properly begin by stating, "What is claimed is." or "I/We claim" because the claims should read in sentence format.

Appropriate correction is required.

Claim Objections

Claims 5, 29, 32, 34-36 and 46-61 are objected to because of the following informalities: the claims contain non-elected subject matter (i.e., the sequences identified as other than SEQ ID NO: 22). Appropriate correction is required.

Claims 57, 59 and 61 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be set forth in the alternative. See MPEP § 608.01(n). Accordingly, the claims 57, 59 and 61 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-30, 32, 34-36, 46-56, 58 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5, 6, 8, 10, 12-14, 16-18, 20, 23-26, 29, 30, 32, 34-36 and 46-56 (and thus their dependent claims) fail to properly begin with an article, such as “A” or “The,” and therefore use improper English Grammar. As a result, it is unclear what is being claimed in the absence of an article to properly identify the claimed invention.

Claim 5 is indefinite because it recites “SEQ ID NO: 8” twice. It is unclear why SEQ ID NO: 8 must be reiterated, although it is noted that the claim does not recite SEQ ID NO: 18. This potential typographical error can be remedied by changing SEQ ID NO: 8 to SEQ ID NO: 18.

Claims 5, 29, 32 and 34 are indefinite because they recite multiple periods in the claims, making it unclear where the claim actually ends. It would be remedial to properly annotate the SEQ ID NOS with a colon following the “NO,” rather than a period.

Claim 46 is indefinite because it recites the term “uence” which is not an English word. It is unclear what this word means, although it is noted that this may be a typographical error for “sequence.”

Claims 52-56, 58, and 60 are indefinite because the claims refer to the method of claim 48 or 49, which are not methods. It is unclear if the claims should properly refer to another method claim, or if the claims should properly be cell claims, which are dependent on the cell set forth in claim 48 or 49.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-28, 30, 35, 36, 46-56, 58 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomas *et al.* (IDS reference # 10; see entire document; henceforth Thomas).

The instant rejection is predicated upon the interpretation of the following terms as set forth in the instant specification:

1. A “P-box” is *any* sequence that directs transcription in endosperm tissue. Such a sequence would be inherently present in a promoter sequence for a gene encoding a high molecular weight glutein (HMWG) such as *Glu-D1-2* or *Dx5*. This interpretation is necessitated by the definition set forth in the specification on page 12; it is noted that the definition set forth in the specification improperly incorporates by reference an element that is central to the determination of patentability.
2. An “as1” and “as2” element are interpreted as being present in any chimeric promoter that includes the CaMV promoter, as both of these sequences originate from the CaMV promoter.
3. A “cereal box” is interpreted as *any* sequence that is present in a functional seed specific promoter/enhancer, there being no structural limitation set forth in the specification to more fully set the metes and bounds of the term “cereal box.”

Based upon the aforementioned interpretations, which are within the teachings of the specification, Thomas anticipates the instant claims. Thomas teaches a chimeric promoter that includes the enhancer region from the promoter of the HMWG gene *Glu-D1-2* (henceforth the HMWG promoter) and a functional portion of the CaMV promoter (see for example the Abstract, Figure 1, etc.). Because the HMWG promoter sequence is specific for expression in wheat seeds (i.e., the promoter is endosperm specific)(see for example the Abstract), it must necessarily comprise a “P-box” as well as a “cereal box”; furthermore, since there is no structural limitation on the term “cereal box,” there are necessarily two such boxes without any intervening sequences. An inspection of the promoter truncation constructs (see for example Table 1) indicates that there are sequences upstream from the functional enhancer element because a truncation of the 3’ region of the HMWG promoter results in at least a partial reduction in the enhanced transcription of the chimeric promoter. Absent any evidence to the contrary, and given the broad interpretation of the term “cereal box,” those upstream sequences comprise “cereal boxes.” Significantly, the HMWG enhancer contains a GATA box (located from -296; see for example the second line of nucleotides set forth in Figure 2), a “G-box” (i.e., a sequence with ACGT as its core; located from -270; see for example the third line of nucleotides set forth in Figure 2), a TATA box (see for example the boxed sequence on the eighth line of the nucleotide sequence set forth in Figure 2) and a GC-rich sequence both 5’ and 3’ to the transcription start site of the sequence (located from -214 and +18, respectively; see for example the fourth and last lines of the nucleotide sequence set forth in Figure 2). As mentioned before, the chimeric promoter also includes sequences from the CaMV promoter, which inherently contains an as1 (conferring root specific expression) and as2 box (conferring photosynthetic tissue expression).

Furthermore, these CaMV sequences are located downstream from the “cereal boxes” and other enhancer elements of the HMWG promoter/enhancer because the CaMV promoter element is structurally located downstream from the HMWG region in the constructs taught by Thomas. These promoter constructs were placed into expression vectors (see for example Figure 1), transformed into tobacco plant cells (as well as *E. coli* for cloning purposes)(see for example page 1177-1178, bridging paragraph), and measured for their ability to express a reporter protein (see for example the results set forth in Table 1). Importantly, constructs pGUS45 and pGUS148 give greater than a 1.5-fold increase in transcription relative to a promoter that does not have the full enhancer element (such as construct pGUS283 or the control plasmid pBl121.5)(see for example the results set forth in Table 1). As a result, Thomas teaches the chimeric promoters claimed in the claims set forth above, both structurally and functionally, thereby anticipating the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (as set forth above in the rejection of claims 1, 2, 6-28, 30, 35, 36, 46-56, 58 and 60 under 35 U.S.C. 102(b)) in view of Halford *et al.* (IDS reference #13; see entire document; henceforth Halford).

Thomas teaches all of the elements set forth above in the rejection of claims 1, 2, 6-28, 30, 35, 36, 46-56, 58 and 60 under 35 U.S.C. 102(b). However, Thomas does not teach the use of the *Glu-1Dx5* promoter, specifically.

Halford teaches a functional analysis of the *Glu-1Ay1* and *Glu-1Dx5* promoter sequence (see for example Figure 3 and Table 1). Halford further teaches that the *Glu-1Dx5* promoter sequence showed enhanced expression as a result of promoter activity (see for example the Abstract, Figure 3, Table 1, and page 212, the paragraph bridging the left and right columns). Finally, Halford teaches that their results suggest, “that the HMW regulatory sequences may be useful for driving high levels of expression in tobacco” (see for example page 214, the paragraph bridging the left and right columns).

It would be obvious for one of ordinary skill in the art to combine the teachings of Thomas and Halford because both teachings involve the expression of heterologous sequences specifically in tobacco using promoters derived from HMWG genes. One of skill in the art would have been motivated to substitute the *Glu-1Dx5* promoter taught by *Glu-D1-2* promoter taught by Thomas because Halford suggests using their particular promoters for the enhanced expression of heterologous genes in tobacco, which is where Thomas is expressing their heterologous gene. Given the teachings of both references, the obviousness of the combination, and the clear motivation to combine the references provided by Halford, the ordinary skilled artisan would have had a reasonable expectation of success when combining the teachings, absent any evidence to the contrary.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636



JAMES KETTER
PRIMARY EXAMINER